REMARKS

Applicants respectfully request entry of the amendments and remarks submitted herein. Applicants have added new claim 33, which is a particular embodiment of the claimed methods. Claim 33 describes an embodiment of the invention in which amplification is used to identify the particular marking nucleic acids that were used to label a substance. Applicants submit that new claim 33 is free from the art cited by the Examiner. For the convenience of the Examiner, the embodiment of new claim 33 is described herein using two real-life scenarios. The embodiments described herein are not intended to limit the interpretation of new claim 33, but are only intended to exemplify the use of the method.

Claims 1-16, 18-27, 29-32 and 33 are currently pending. Reconsideration of the pending application is respectfully requested.

Representative Examples of the Method of New Claim 33

A. The first example is derived from a proposal submitted to a governmental agency outside of the U.S. for a method of labeling and being able to subsequently identify any of 50 different petrol products (e.g., for taxation purposes). For this method, 50 different marking nucleic acids were designed having the following configuration:

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first primer binding site *identification sequence$_{1-50}$* *second primer binding site*

In this example, 50 different identification sequences are designed with each different identification sequence flanked by the same first primer binding site and second primer binding site. The identification sequences are designed such that they have similar melting temperatures but that cross-hybridization does not occur between or within members of the marking nucleic acids and/or the resulting amplification product(s). Using such a design strategy allows one to use the same conditions in the amplification and detection reactions for all 50 different marking nucleic acids.

For labeling the petrol products, each petrol product is mixed with one of the defined marking nucleic acids at a concentration of, for example, 1 pM.

To identify a particular petrol product, the marking nucleic acid in a particular sample of petrol is isolated and amplified using primers that bind to the first and second primer binding sites. One or both of the primers can include, for example, a fluorophore such that the amplification product is fluorescently labeled. The particular amplification product is then identified by, for example, hybridization to a DNA chip upon which each of the 50 different identification sequences is immobilized at a defined position. The particular petrol product is identified by determining which identification sequence on the DNA chip hybridizes to the fluorescently labeled amplification product.

B. The second example is derived from a proposal for a method of marking and identifying 25,000 different fragrance bottles such that the company manufacturing such fragrance bottles could control the growth of their products. The company wanted the ability to trace every bottle of fragrance from each production run, with each production run consisting of 25,000 bottles. This proposal requires a more complex strategy for differentially labeling such a large number of individual products. Therefore, a similar group of marking nucleic acids similar to those described above in Example A were designed and each fragrance bottle was labeled with multiple marking nucleic acids. For example, if each fragrance bottle were labeled with a non-repetitive combination of 5 different marking nucleic acids, a total of at least 22 different identification sequences (e.g., identification sequence$_{1-22}$) would be required, whereas if each fragrance bottle were labeled with 10 different marking nucleic acids, a total of at least 18 different identification sequences (e.g., identification sequence$_{1-18}$) would be required.

For identification, the marking nucleic acids from a bottle of fragrance are isolated and amplified with primers that bind to the first and second primer binding site as described above in Example A. Also as described above, the particular pattern of amplification products is identified using a DNA chip, which allows for identification (and authentication) of any of the fragrance bottles.

The 35 U.S.C. §102 Rejections

Claims 1, 7-10, 13-15, 18, 20-23, and 27 stand rejected under 35 U.S.C. §102(b) as being anticipated by Cantor et al. (U.S. Patent No. 5,795,714). In response to Applicants' arguments that the random sequences used and disclosed by Cantor et al. would not be used in the claimed

methods, the Examiner asserted that this argument is not persuasive because the claims do not require that the sequence is not random. The Examiner asserted that "a predefined nucleic acid molecule does not mean that the sequence of the nucleic acid is known or non-random," and that "predefined means to define beforehand." The Examiner asserted that the claim only requires that the nucleic acid molecule is defined beforehand, which, according to the Examiner, could be interpreted to mean any group of nucleic acids which are selected to be used in the assay. This rejection is respectfully traversed.

According to independent claims 1 and 27, a first group of *predefined* nucleic acid molecules is provided. As disclosed in the specification (see, for example, page 2, lines 31-37 and page 3, lines 31-33), the first group of nucleic acid molecules is "predefined" in that each member of the first group of nucleic acid molecules includes an (known) identification sequence section which is complementary to a (known) detection sequence section of each member of the second group of nucleic acid molecules. Therefore, the first group and the second group of claimed nucleic acids have an identical number of different members, the sequences all of which are known and specifically designed toward one another. The word in the originally-written German application that was translated into the claim term "predefined" was "vorgegeben." In addition to "predefined," the German word "vorgegeben" also translates into the English words "default," "given," "predetermined," and "specified." See the attached printout from an online dictionary (http://dict.leo.org). It is Applicants' position that a sequence must be "known" in order to be "specified" or "predetermined," and, therefore, a "known" sequence is the opposite of a "random" sequence. Applicants assert that the claim term "predefined" does mean "known" and "nonrandom," but if the Examiner would prefer one of the other translations of "vorgegeben," Applicants would likely agree to such an amendment.

The Examiner also asserted that "the claims do not require that identification of a substance occurs, the claims require only that IF hybridization occurs then [identification of] the substance occurs." The Examiner asserted that because the claims recite a final process step of when hybridization does not occur, then the substance is not identified, that the claims do not require that the substance be identified and, therefore, the cited reference does teach the claimed method. Applicants have amended claims 1 and 27 to clarify that not necessarily all of the IDS1-n and IDP1-n need to hybridize for identification to occur. As exemplified above, it is the

particular pattern of IDS1-n and IDP1-n that hybridize that allow identification or authentication of the substance.

In view of the remarks herein, Applicants respectfully request that the rejection of claims 1, 7-10, 13-15, 18, 20-23, and 27 under 35 U.S.C. §102(b) be withdrawn.

Claims 1-15, 18-23, 27, and 29-32 stand rejected under 35 U.S.C. §102(b) as being anticipated by Lizardi et al. (U.S. Patent No. 5,854,033). The Examiner asserted that Lizardi et al teach a method for detection of target nucleic acid sequences and correlated this with the claimed method of identifying a substance. The Examiner equated the open circle probe of Lizardi et al. with the claimed predefined nucleic acid molecule having an identification sequence section. The Examiner also asserted that Lizardi et al. incubates the probe with a target sample (which the Examiner equates to the claimed substance) to promote hybridization, which is the equivalent of the claimed contacting and labeling step. This rejection is respectfully traversed.

Lizardi et al. discloses plasmids that can be used in a reporter system that utilizes rolling circle replication. Contrary to the Examiner's assertion, the reporter system of Lizardi et al. has nothing to do with the methods of independent claims 1, 27, 31, and 32. Lizardi et al. does not teach or suggest the claimed methods of labeling and identifying a liquid, gaseous or solid substance (e.g., claims 1 and 31) or the claimed methods of identifying a labeled liquid, gaseous or solid substance (e.g., claims 27 and 32) where the claimed methods use a first and a second group of nucleic acids, wherein each of the members of one group of nucleic acids has an identification sequence section and each of the members of the other group of nucleic acids has a detection sequence section. Lizardi et al. does not teach or suggest the steps and features of the claimed methods.

In view of the remarks herein, Applicants respectfully request that the rejection of claims 1-15, 18-23, 27, and 29-32 under 35 U.S.C. §102(b) be withdrawn.

The 35 U.S.C. §103 Rejections

Claims 1, 2, 6, 16, 18, 24, and 25 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Bumstead et al. (*J. Virological Methods*, 65:75-81, 1997) in view of Pastinen

et al (*Human Mol. Genetics*, 13(7):1453-1462, 1998). The Examiner asserted that Bumstead et al. teach a quantitative assay to determine the number of viral genomes present in samples using PCR amplification of the viral genome and fluorescent-tagged primers. The Examiner admits that Bumstead et al. does not teach a second set of nucleic acid molecules on a solid support. The Examiner asserted that Pastinen et al. teaches an array-based multiplex analysis of candidate genes, and that multiplex genotyping and the miniaturized assay format has the advantage of small reaction volumes, fast reaction rates, and easy handling of multiple samples in parallel.

The Examiner concluded that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to improve on the method of Burman et al. (to determe the number of viral genomes present in a sample using PCR amplification with fluorescent-tagged primers) to include the array analysis as taught by Pastinen. The Examiner asserted that the motivation to combine the two references can be found in Pastinen et al. because Pastinen et al. teaches that multiplex genotyping and miniaturized assay format has several advantages. The Examiner also asserted that the references provide a reasonable expectation of success because both Burman et al. and Pastinen et al. use PCR amplification to identify genes and Pastinen et al. teaches that an array allows for easy handling of multiple samples in parallel. Applicants respectfully traverse this rejection.

Applicants submit that the claimed invention is not obvious in view of the cited references. Instead, it is Applicants' own disclosure that the Examiner is employing to reach the claimed invention. The Examiner is respectfully reminded that any teaching or suggestion of obviousness must be found in the cited art, and that it is impermissible to use the Applicants' own disclosure to provide the basis for a *prima facie* case of obviousness. The legal standard applicable to determinations under 35 USC. §103 based on a combination of references was stated by the Court of Appeals for the Federal Circuit in *In re Dow Chemical Co.*, 837 F2d 469, 472-473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988):

> The consistent criterion for determination of obviousness is whether the prior art would suggest to one of ordinary skill in the art that this process shall be carried out and would have a reasonable expectation of success, viewed in the light of the prior art. Both the suggestion and the expectation of the success must be found in the prior art, not in applicant's disclosure. [Citation omitted; emphasis added].

An invention is not obvious merely because the prior art could be modified. *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Instead, the prior art, as a whole, must fairly suggest the desirability to make the applicants' invention. *Id.* The simple advantages disclosed in Pastinen et al. are not sufficient to provide motivation to combine the two references.

Neither of the references, alone or in combination, teach or suggest using a first group of predefined nucleic acids and a second group of nucleic acids that, for every member, has a corresponding member in the first group of nucleic acids that is complementary to a member in the second group. Furthermore, embodiments such as those in dependent claims 2 and 6, for example, in which each member of the first group of nucleic acids contains primer binding sites flanking the identification sequence and amplification is used to identify the substance, is not taught or suggested by the cited references or a combination thereof.

In view of the amendments and remarks herein, Applicants respectfully request that the rejection of claims 1, 2, 6, 16, 18, 24, and 25 under 35 U.S.C. §1030(a) be withdrawn.

CONCLUSION

In view of the amendments and remarks herein, Applicants respectfully request that claims 1-16, 18-27, 29-32 and 33 be allowed. Specifically, Applicants submit that new claim 33 is free from the art cited above and should be allowed. Please apply the fee for the Extension of Time and any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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